

***What Is Claimed Is:***

1. An isolated polypeptide comprising an amino acid sequence at least 95% identical to Gly (138) - Ser (208) of SEQ ID NO:2.

2. The isolated polypeptide of claim 1, wherein said amino acid sequence is at least 95% identical to Val (123) - Ser (208) of SEQ ID NO:2.

3. The isolated polypeptide of claim 2, wherein said amino acid sequence is at least 95% identical to Glu (104) - Ser (208) of SEQ ID NO:2.

4. The isolated polypeptide of claim 3, wherein said amino acid sequence is at least 95% identical to Val (77) - Ser (208) of SEQ ID NO:2.

5. The isolated polypeptide of claim 4, wherein said amino acid sequence is at least 95% identical to Ser (69) - Ser (208) of SEQ ID NO:2.

6. The isolated polypeptide of claim 5, wherein said amino acid sequence is at least 95% identical to Ala (63) - Ser (208) of SEQ ID NO:2.

7. The isolated polypeptide of claim 6, wherein said amino acid sequence is at least 95% identical to Cys (37) - Ser (208) of SEQ ID NO:2.

8. The isolated polypeptide of claim 7, wherein said amino acid sequence is at least 95% identical to Thr (36) - Ser (208) of SEQ ID NO:2.

9. The isolated polypeptide of claim 8, wherein said amino acid sequence is at least 95% identical to Trp (2) - Ser (208) of SEQ ID NO:2.

10. The isolated polypeptide of claim 9, wherein said amino acid sequence is at least 95% identical to Met (1) - Ser (208) of SEQ ID NO:2.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to Ala (63) - Lys (153) of SEQ ID NO:2.

12. The isolated polypeptide of claim 11, wherein said amino acid sequence is at least 95% identical to Thr (36) - Lys (153) of SEQ ID NO:2.

13. An isolated polypeptide comprising Gly (138) - Ser (208) of SEQ ID NO:2.

14. The isolated polypeptide of claim 13, which comprises Val (123) - Ser (208) of SEQ ID NO:2.

15. The isolated polypeptide of claim 14, which comprises Glu (104) - Ser (208) of SEQ ID NO:2.

16. The isolated polypeptide of claim 15, which comprises Val (77) - Ser (208) of SEQ ID NO:2.

17. The isolated polypeptide of claim 16, which comprises Ser (69) - Ser (208) of SEQ ID NO:2.

18. The isolated polypeptide of claim 17, which comprises Ala (63) - Ser (208) of SEQ ID NO:2.

19. The isolated polypeptide of claim 18, which comprises Cys (37) - Ser (208) of SEQ ID NO:2.

20. The isolated polypeptide of claim 19, which comprises Thr (36) - Ser (208) of SEQ ID NO:2.

21. The isolated polypeptide of claim 20, which comprises Trp (2) - Ser (208) of SEQ ID NO:2.

22. The isolated polypeptide of claim 21, which comprises Met (1) - Ser (208) of SEQ ID NO:2.

23. An isolated polypeptide comprising Ala (63) - Lys (153) of SEQ ID NO:2.

24. The isolated polypeptide of claim 23, which comprises Thr (36) - Lys (153) of SEQ ID NO:2.

25. An isolated polypeptide consisting essentially of an amino acid sequence at least 95% identical to Ser (69) - Ser (208) of SEQ ID NO:2.

26. The isolated polypeptide of claim 25, wherein said amino acid sequence is at least 97% identical to Ser (69) - Ser (208) of SEQ ID NO:2.

27. The isolated polypeptide of claim 26, wherein said amino acid sequence is at least 99% identical to Ser (69) - Ser (208) of SEQ ID NO:2.

28. An isolated polypeptide consisting essentially of Ser (69) - Ser (208) of SEQ ID NO:2.

29. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, or 25, having a Met residue at the N-terminus.

30. The isolated polypeptide of claim 28, having a Met residue at the N-terminus.

31. The isolated polypeptide of claim 1 or 13, wherein said amino acid sequence includes one or more amino acid substitutions selected from Gly (142) Ala, Ser (143) Lys, Phe (146) Ser, Asn (148) Glu, Lys (151) Asn, Leu (152) Phe, Glu (154) Gly, Glu (154) Asp, Arg (155) Leu, Glu (157) Leu, Gly (160) His, Phe (167) Ala, Asn (168) Lys, Gln (170) Thr, Arg (174) Gly, Tyr (177) Phe, Gly (182) Gln, Ala (185) Val, Ala (185) Leu, Ala (185) Ile, Arg (187) Gln (190) Lys, Lys (195) Glu, Thr (197) Lys, or Ser (198) Thr.

32. The isolated polypeptide of claim 5, 17, 25, or 28 wherein said amino acid sequence includes one or more amino acid substitutions selected from Trp (79) Val, Arg (80) Lys, Lys (87) Arg, Tyr (88) Trp, Phe (89) Tyr, Lys (91) Arg, Ser (99) Lys, Lys (102) Gln, Lys 103(Glu), Glu (104) Met, Asn (105) Lys, Pro (107) Asn, Ser (109) Asn, Leu (111) Met, Thr (114) Arg, Glu(117) Ala, Val (120) Ile, Val (123) Ile, Ala (125) Gly, Ile (126) Val, Asn (127) Glu, Asn (127) Gln, Tyr (130) Phe, Met (134) Thr, Lys (136) Glu, Lys (137) Glu, Gly (142) Ala, Ser (143) Lys, Phe (146) Ser, Asn (148) Glu, Lys (151) Asn, Leu (152) Phe, Glu

(154) Gly, Glu (154) Asp, Arg (155) Leu, Glu (157) Leu, Gly (160) His, Phe (167) Ala, Asn (168) Lys, Gln (170) Thr, Arg (174) Gly, Tyr (177) Phe, Gly (182) Gln, Ala (185) Val, Ala (185) Leu, Ala (185) Ile, Arg (187) Gln (190) Lys, Lys (195) Glu, Thr (197) Lys, Ser (198) Thr, Arg (194) Glu, Arg (194) Gln, Lys (191) Glu, Lys (191) Gln, Arg (188) Glu, Arg (188) Gln, or Lys (183) Glu.

33. The isolated polypeptide of claim 11 or 23, wherein said amino acid sequence includes one or more amino acid substitutions selected from Ala (63) Pro, Gly (64) Glu, Val (67) Thr, Trp (79) Val, Arg (80) Lys, Lys (87) Arg, Tyr (88) Trp, Phe (89) Tyr, Lys (91) Arg, Ser (99) Lys, Lys (102) Gln, Lys 103(Glu), Glu (104) Met, Asn (105) Lys, Pro (107) Asn, Ser (109) Asn, Leu (111) Met, Thr (114) Arg, Glu(117) Ala, Val (120) Ile, Val (123) Ile, Ala (125) Gly, Ile (126) Val, Asn (127) Glu, Asn (127) Gln, Tyr (130) Phe, Met (134) Thr, Lys (136) Glu, Lys (137) Glu, Gly (142) Ala, Ser (143) Lys, Phe (146) Ser, Asn (148) Glu, Lys (151) Asn, or Leu (152) Phe.

34. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, 25, or 28, which is part of a fusion protein.

35. The isolated polypeptide of claim 34, wherein said polypeptide is fused to a marker.

36. The isolated polypeptide of claim 35, wherein said marker is selected from the group consisting of a hexahistidine tag and a hemagglutinin tag.

37. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, 25, or 28, which stimulates proliferation of epithelial cells.

38. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, 25, or 28, which stimulates proliferation of keratinocytes.

39. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, 25, or 28, which is produced in a recombinant host cell.

5 40. The isolated polypeptide of claim 39, wherein said host cell is mammalian.

41. The isolated polypeptide of claim 39, wherein said host cell is bacterial.

10 42. The isolated polypeptide of claim 41, wherein said host cell is *E. coli*.

43. An isolated polypeptide comprising a hydrophilic region of Keratinocyte Growth Factor-2 (KGF-2) selected from the group consisting of Gly (41) - Asn (71), Lys (91) - Ser (109), Asn (135) - Tyr (164), and Asn (181) - Ala (199) of SEQ ID NO:2.

15 44. The polypeptide of claim 43, which is not more than 100 amino acids in length.

45. The polypeptide of claim 44, which is not more than 50 amino acids in length.

46. The isolated polypeptide of any one of claims 1, 5, 11, 13, 17, 23, or 25, together with a pharmaceutically acceptable carrier or excipient.

47. The isolated polypeptide of claim 28, together with a pharmaceutically acceptable carrier or excipient.

5 48. An isolated polynucleotide encoding a polypeptide of any one of claims 1, 5, 11, 13, 17, 23, 25, or 28.

49. The isolated polynucleotide of claim 48, which is optimized for expression in *E. coli*.

10 50. The isolated polynucleotide of claim 49, having the nucleotide sequence of SEQ ID NO:38.

51. The isolated polynucleotide of claim 49, having the nucleotide sequence of SEQ ID NO:42.

52. The isolated polynucleotide of claim 49, having the nucleotide sequence of SEQ ID NO:54.

15 53. The isolated polynucleotide of claim 49, having the nucleotide sequence of SEQ ID NO:111.

54. A method for making a recombinant vector comprising inserting the polynucleotide of claim 48 into a vector.

55. A recombinant vector produced by the method of claim 54.

56. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 55 into a host cell.

57. A recombinant host cell produced by the method of claim 56.

58. The isolated polypeptide of claim 1, 5, 11, 13, 17, 23, 25, or 28, which is produced by a method comprising:

introducing a recombinant vector comprising a polynucleotide encoding said polypeptide into a host cell;

culturing said host cell; and

recovering said polypeptide.

59. A method for producing a polypeptide comprising:

culturing the recombinant host cell of claim 57 under conditions that said vector is expressed; and

recovering said polypeptide.

60. A method of stimulating proliferation of epidermal cells comprising administering an effective amount of the polypeptide of claim 1.

61. The method of claim 60, wherein the epidermal cells are keratinocytes.



62. The method of claim 61, wherein said polypeptide is administered to an individual.

63. The method of claim 62, wherein said polypeptide is administered for a purpose selected from: preventing or improving the appearance of wrinkles or aged skin, improving skin strength, promoting epidermal thickening, reducing scarring, or improving healing after cosmetic surgery.

64. A method of stimulating proliferation of epithelial cells comprising administering an effective amount of the polypeptide of claim 1.

65. The method of claim 64, wherein said epithelial cells are selected from epithelial cells of the liver, pancreas, kidney, prostate, bladder, lung and esophagus.

66. A method of promoting wound healing comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

67. The method of claim 66, wherein said individual is wound healing impaired.

68. The method of claim 67, wherein said impairment in wound healing is caused by diabetes, ischemic blockage or injury, steroids, non-steroid compounds, uremia, malnutrition, vitamin deficiencies, obesity, infection, immunosuppression, radiation therapy, or chemotherapy.

69. The method of claim 66, wherein said wound is selected from surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, or burns.

70. A method of treating wounds caused by a colonic or gastrointestinal (GI) surgical procedure comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

71. The method of claim 70, wherein said procedure is anastomosis.

72. The method of claim 70, wherein said individual is wound healing impaired.

73. The method of claim 72, wherein said impairment is caused by diabetes, ischemic blockage or injury, steroids, non-steroid compounds, uremia, malnutrition, vitamin deficiencies, obesity, infection, immunosuppression, radiation therapy, or chemotherapy.

74. A method of treating or preventing mucositis comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

75. The method of claim 74, wherein said mucositis is selected from oral, esophageal, gastric, intestinal, colonic, rectal or anal.

76. A method of treating inflammatory bowel disease comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

77. The method of claim 76 wherein said disease is selected from ulcerative colitis or Crohn's disease.

78. A method of reducing inflammation comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

79. The method of claim 78, wherein said inflammation is associated with a disease or condition selected from psoriasis, eczema, dermatitis, or arthritis.

80. A method of promoting hair growth comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

81. A method of treating tissue exposed to radiation or protecting tissue to be exposed to radiation comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

82. The method of claim 81, wherein said polypeptide is administered to allow an increase in radiation dosage used to treat a malignancy in said individual.

83. The method of claim 82, wherein said polypeptide is administered to treat a radiation-induced condition selected from oral injury, gastro-intestinal injury, mucositis, intestinal fibrosis, proctitis, pulmonary fibrosis, pneumonitis, pleural retraction, hemopoietic syndrome, or myelotoxicity.

5 84. A method of promoting urothelial healing comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

10 85. A method of promoting tissue growth or repair in the female genital tract comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

15 86. A method of treating or preventing viral hepatitis comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

20 87. A method of treating or preventing liver failure comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

88. The method of claim 87, wherein the liver failure is caused by a disease or condition selected from acute viral hepatitis, cirrhosis, drug-induced hepatitis, toxin-induced hepatitis, autoimmune chronic active hepatitis, liver transplantation, or partial hepatectomy.

89. The method of claim 88, wherein said toxin-induced hepatitis is caused by a hepatotoxin selected from acetaminophen, carbon tetrachloride, methotrexate, or an organic arsenical.

5 90. A method of treating or preventing pancreatitis comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

10 91. A method of treating or preventing a lung damaging condition comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof. *B*

15 92. The method of claim 91, wherein the condition is selected from emphysema, inhalation injury, chemotherapy, radiation treatment, lung cancer, asthma, respiratory distress syndrome, or bronchopulmonary dysplasia.

93. A method of treating or preventing renal failure comprising administering an effective amount of the polypeptide of claim 1 to an individual in need thereof.

94. An isolated polypeptide consisting of Met (1) - Ser (141) in SEQ ID NO:96.

*Add B<sub>1</sub>*